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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,215	10/26/2001	Kevin K. Liu	PC11053AMAG	8104

7590 03/26/2003

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EXAMINER
LIU, HONG

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,215	LIU ET AL.	
	Examiner	Art Unit	
	Hong Liu	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-41 is/are pending in the application.

4a) Of the above claim(s) 7-11,14-17,21-26 and 30-41 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-6,12,13,18-20 and 27-29 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1 .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Claims 1-41 are pending in this application.

Election/Restrictions

I. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-29, drawn to the compounds of formula I where in R4 is alkyl-het or R3 and R4 are taken together with N to form het, the compositions and methods of use, classified in classes 544, 546, and 548 and subclasses depending on the type of het rings.

II. Claims 1-29, drawn to the compounds of formula I where in R4 is hydrogen or alkyl-NR5R6, the compositions and methods of use, classified in class 560, subclasses134.

III. Claims 30-36 and 39, drawn to the methods of treatment of glucocorticoid receptor mediated diseases comprising administrating the compounds and another pharmaceutical agent, classified in class 514, subclass 418.

IV. Claim 37, drawn to a kit, classified in class 206, subclass 569.

V. Claims 38, drawn to a method of inducing weight loss, classified in class 514, subclass 418.

VI. Claims 40 and 41, drawn to a method of treating an inflammatory disease, classified in class 514, subclass 418.

II. The inventions are distinct, each from the other because of the following reasons:

Groups I-II are directed to structurally dissimilar compounds such that the variables created by varying the definitions of R3 amd R4 do not belong to a recognized class of chemical compounds in the art, and references anticipating one invention would not render obvious the others, for example, carbamic acid is different from a heterocyclic ring such as piperidine or piperazine. Thus, separate searches in the literature as well as in the U.S. Patent Clarification System would be required. Each group's compounds are made and used independently of each other and could support separate patents. The compounds differ significantly in chemical structures. One skilled in the art would not consider such diverse structures as functional equivalents of each other. The mere fact that there is a single similarity is not in itself a significant reason to render the whole embodiment obvious.

III. Inventions I-II and III-VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case more than one use exists for compounds of Group I as evidenced by claims 30-41 drawn to a variety of diverse uses. Additionally, the various uses would raise issues of enablement separate from that of the compound claims and would require art-recognized evidence that activity relied on its reasonably correlated to in vivo efficacy for the uses claimed.

During a telephone conversation with Ms. Martha Gammill on 03/17/03 a provisional election was made with traverse to prosecute the invention of Group II, claims 1-29. Affirmation of this election must be made by applicant in replying to this Office action. Claims 7-11, 14-17, 21-26, and 30-41 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

IV. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 1-3 are objected as being an improper Markush grouping. The recited compounds, while possessing a common utility, present a variable core and, thus, the Markush groups represented by the term where R4 is carbamic and R4 is a heterocyclic ring or R3 and R4 form a heterocyclic ring have variably different definitions, render the claims clearly improper.

Deletion of non-elected subject matter would overcome this rejection.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-6 and 27-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparation of compounds wherein R2 is alkyl or phenyl,

does not reasonably provide enablement for preparation and use of compounds wherein R2 is a functional group other than the above specified functional groups. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein R2 can be alkyl or phenyl substituted with Z-het which is an unsubstituted or substituted, aromatic or an unsubstituted or substituted, heteroaromatic group, containing one or more heteroatoms, etc. While many compounds are disclosed, there is insufficient guidance for preparing additional glucocorticoid receptor modulators which would be effective since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants' claims. Only compounds wherein R2 is phenyl or unsubstituted alkyl have been made.

Furthermore, testing data is limited to a number of compounds not considered to be representative of all the possible compounds encompassed by the claims. Examples should be of sufficient scope as to justify the scope of the claim. However, the generic claims are much broader in scope than is represented by the testing. The definitions of the various R2 variables embrace many structurally divergent groups not represented at all in testing, since testing for the instant compounds is not seen in the specification. Markush claims must be provided with support in the disclosure when the "working examples' fail to include written description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See In re Fouch, 169 USPQ 429.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds embraced by the claims which have not been tested. In cases directed to chemical compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made that the instant compounds as an entire class have the required activities needed to practice the invention. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability" have been demonstrated to be sufficiently lacking in the instant case for the scope being claimed.

Claims 1, 2, and 27 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of "prodrug" is not adequately enabled. Applicants provide no guidance as how the compounds are made more active in vivo. The choice of a "prodrug" will vary from drug to drug. Therefore, more than minimal routine experimentation would be required to determine which prodrug will be suitable for the instant invention.

Claims 27, along with claims 28-29, is drawn to methods of treatment of glucocorticoid receptor-mediated diseases. This claim is interpreted to include any and all disorders associated with this particular mode of action. The specification reads on any and all diseases such as

obesity, diabetes, depression, anxiety, and neurodegereation. However, in a recent review article, Pariante and Miller showed that glucocorticoid receptors are only implicated in depression (See abstract, J. Biol. Psychiatry, 2001). Furthermore, no evidence of in vitro/in vivo effectiveness is seen in the specification for one (let alone all) of the instant compounds for the uses claimed herein. See In re Surrey, 252 USPQ 724, regarding sufficiency of disclosure. Competent evidence of art-recognized efficacy for intended uses needs to be provided. Any evidence presented must be commensurate in scope with the claims and must clearly demonstrate the likelihood of in vivo use for all uses being claimed. See Ex parte Powers, 220 USPQ 925.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 27 is of indeterminate scope for more than one reason. First, no one particular disorder is recited. Second, the claim language may read on diseases not yet fully understood to be affected by glucocorticoid receptor modulation.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-6, 12, 13, 18-20, and 27-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 9, 10, 62, and 73 of copending Application No. 10/080,174. Although the conflicting claims are not identical, they are not patentably distinct from each other because there are overlapping subject matter, in particular, when the reference compound is of formula II wherein R10 is –O-Z-C(O)-NR12R13 wherein R12 and R13 is alkyl.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Liu whose telephone number is 703 3065814. The examiner can normally be reached on 8:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703 308 4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703 308-4556 for regular communications and 703 3084734 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 358-1235.

Mukund Shah
Supervisory Patent Examiner
Art Unit 1624

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March 20, 2003

JOHN M. FORD
PRIMARY EXAMINER
GROUP - ART UNIT 1624